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BRAIN AND BEHAVIOUR: A GORDIAN KNOT?

by

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1. INTRODUCTION

As a result of initiatives taken by Gerard Baerends, work in this department on problems in the borderland between ethology and physiology began in 1952. Of the various lines into which it has branched only one will be discussed here. This aims at explaining in physiological terms the more or less patterned succession of activities exhibited by animals under natural conditions. This work follows ethological usage in that a) it views the behavioural repertoire of the individual as a set of discrete elementary activities, and b) it postulates a causal relation between current external stimulation and the overt performance of these elements.

In '*The Study of Instinct*' Niko Tinbergen has stated that "instinctive behaviour had usually been classified according to the various biological ends it serves", but that "this classification runs parallel to a classification based on the underlying neurophysiological mechanisms" (TINBERGEN, 1952: 157). When we began our work, we adopted this view as a guiding principle, though rather than Tinbergen's term 'instinct' we used 'behaviour system' to indicate a class of behaviour elements.

Tinbergen emphasized the 'hierarchical' organization of behaviour and postulated a corresponding structure of its neurophysiological mechanisms. Fig. 1 illustrates his conception of such a mechanism, a 'brain centre', at a given level in the hierarchy: a network of neurons whose excitatory state (set by a complex of 'motivational' inputs) governs the readiness of the individual to perform any element of a well defined subset of the behavioural repertoire, in response to the appropriate external stimulus. Such a subset we called a 'behaviour system'. It will become clear below (section 4.1 and 5) that later development of our work has led us away from these views to some extent. Therefore we shall not try to give a more precise definition of 'behaviour system', nor elaborate other aspects of Tinbergen's model of behaviour.

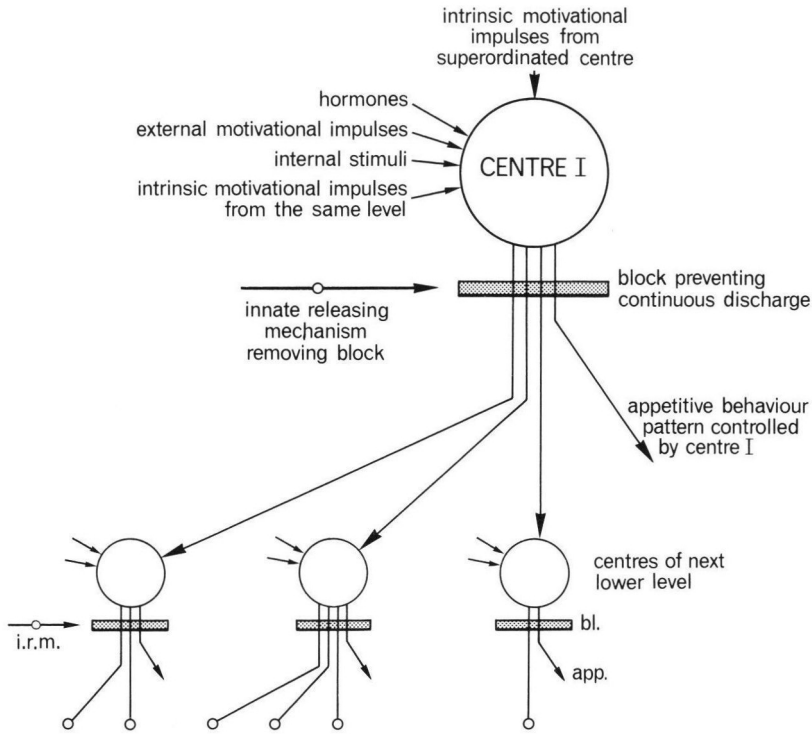

Fig. 1. N. Tinbergen's representation of an 'instinctive centre' at an intermediate level, with its subordinated mechanisms. In Tinbergen's view, the 'innate releasing mechanism' must remove a block that otherwise prevents overt manifestation of the centre's activity. The releasing mechanism acts in response to an external 'key stimulus'. The small circles at the botton of the diagram denote elementary activities. See also text. (From N. TINBERGEN, 1952.)

We shall also sidestep the problem of the distinction between "learning" and "motivation" (DE RUITER, 1967). This is permissible for the moment (see also section 4.1) because most of the experiments reported below were made in constant environments. This implies that, under any common sense definition, the animals had attained a steady state as regards learning, so that variations in their behaviour may provisionally be ascribed to motivational causes. However, in sections 3.2.2. and 4.2.3. we shall make special mention of learning and its interaction with motivation.

In any case we set out to identify the motivational signals as conceived by Tinbergen, and to locate and unravel the functioning of the neural mechanisms on which they impinge. Fruitful as we have found

this approach, we have been able to complete only part of the task in thirty years, for the problems are truly immense. Can they be solved at all, or are we dealing with a real Gordian knot? In this paper we give some examples of results achieved, obstacles encountered, and possible routes for further exploration. These examples are taken only from the work of members of our own team.[1])

2. IN SEARCH OF MOTIVATIONAL MESSAGES: REGULATION OF FOOD INTAKE

2.1. *Starting Point*

From the first we found feeding behaviour a promising subject, for it was known already in the fifties that elimination of the ventromedial hypothalamus (VMH) induces hyperphagia in mammals, whereas elimination of the lateral hypothalamus (LH) causes aphagia. In this light the LH was regarded as a 'hunger centre', mediating between perception of food and performance of feeding responses, and the VMH as a 'satiety centre', recording the energy content of the body and inhibiting the LH as soon as energy exceeds the desired level (fig. 2). However, what satiety signals the VMH received was not yet clear. We shall now discuss how we tried to clarify this, taking examples from our own work without regard to its historical order. We shall not attempt to summarize the vast amount of work done by others on this problem (for a survey, see NOVIN *et al.*, 1976; SILVERSTONE, 1976).

2.2 *Humoral Satiety Signals*

Electrical LH stimulation induces stimulus bound feeding in the rat. When stimulation is given for half an hour every day during some weeks, the animal eats more than its normal intake for a whole day during these 30 minutes (STEFFENS, 1975). As a result it grows more and more obese (fig. 3). Over the same period, spontaneous food intake outside the sessions wanes and eventually ceases completely. After the final stimulation day, the rat continues to eat little for the next few days. Its body weight drops, and its food intake rises, until both regain values customary for rats of that age under ad lib conditions. These findings provide evidence that there is homeostasis of

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[1]) The names of all members of the departmental academic staff who have participated in the team can be found in the list of references (which gives only a selection of key papers). The contributions to our work of graduate students, too numerous to list, and the unfailing support of the technical and secretarial staff are gratefully acknowledged.

body energy, and that this is mediated at least to a large extent by feeding behaviour[1]), but they do not reveal the nature of the satiety signal.

Some clue on the latter point comes from experiments with parabiotic rats (PARAMESWARAN *et al.*, 1977). Between the members of a parabiotic pair, artificial Siamese twins, there is a slow exchange of extracellular fluid (about 1% per minute), but their nervous systems are fully separate. Normally each twin eats its usual daily ration, and maintains a steady body weight. If one of them is subjected to LH stimulation as described above, it overeats and grows fat. Over the

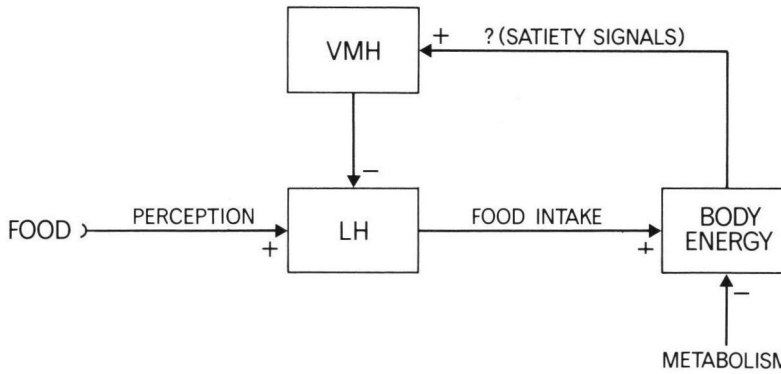

Fig. 2. Simplified model of the control of feeding behaviour. See text.

same period the other twin gradually decreases its intake and grows thinner and thinner (fig. 4). Moreover, it actively avoids contact with food (see section 3.1.2.2.). Although further ethological work may be needed to make fully sure that the thin rat's behaviour is not hampered by its unwieldy partner, we believe that it is the body fluid it receives from the fat one that inhibits its feeding behaviour, though the fluid exchange is too slow for the fuel transferred thereby to cover the thin one's energy expenditure.

What is the nature of the inhibiting agent? In our attempts to identify it we — and others — have paid special attention to blood sugar and its attendant hormone insulin, for glucose is a prime source of energy for the body. A rat under continuous infusion of insulin (STEF-

[1]) Modulation of energy expenditure also contributes to homeostasis, at least in the sense that expenditure is reduced (partly by behavioural means) during food scarcity (WESTERTERP, 1977).

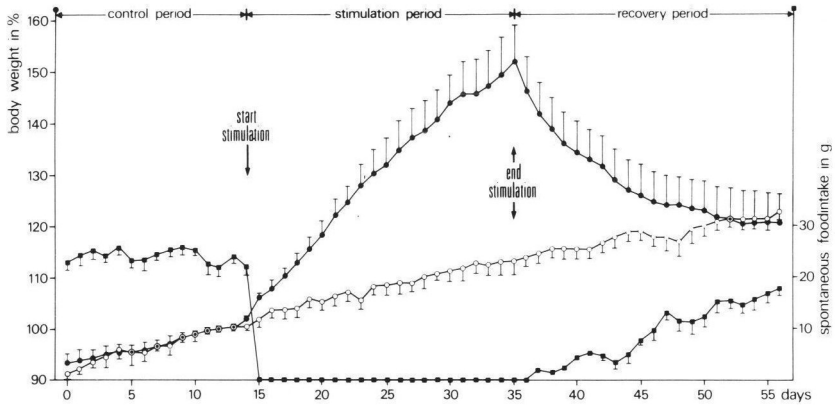

Fig. 3. Mean and S.E.M. of body weight (●) and spontaneous daily food intake (■) of 8 rats subjected from day 15 through 35 to 30 min. electrical LH stimulation. For comparison mean body weight of 4 non-stimulated controls (○) is added. (From STEFFENS, 1975.)

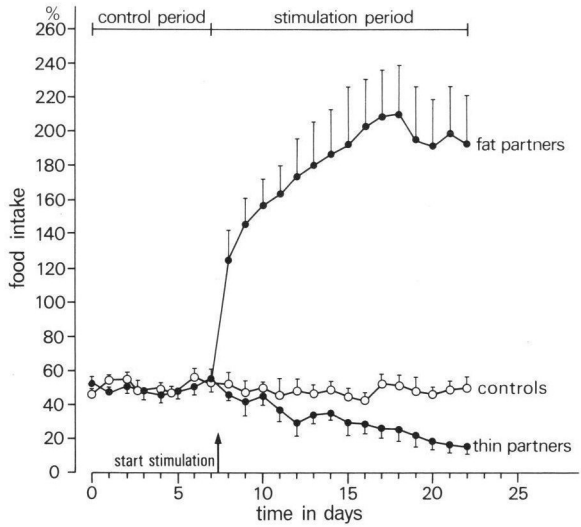

Fig. 4. Daily food intake (means and S.E.M.) of individual parabiotic rats: ○—○ control pairs; ●—● experimental pairs (arrow marks start of daily stimulation of one member). In the absence of stimulation, intake of each member of a pair is estimated at 50% of the total intake of the pair. In the stimulation period, when the intake of each can be measured separately, this is expressed as a percentage of the pair's prestimulation total intake. (From PARAMESWARAN *et al.*, 1977.)

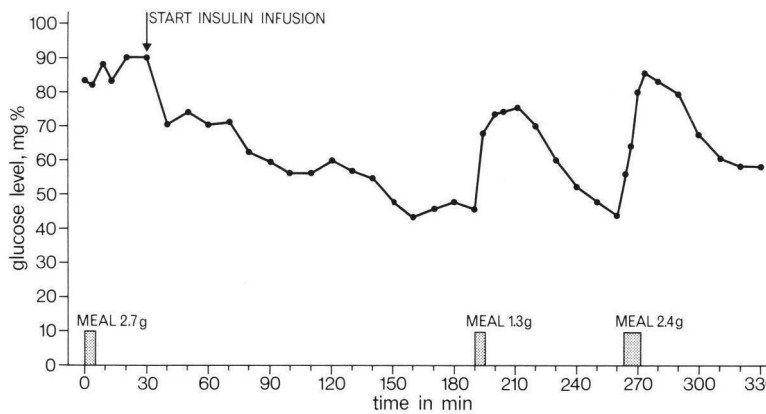

Fig. 5. Meal pattern and blood glucose concentration (mg per 100 ml) in a rat subjected to continuous infusion of insulin at a rate of 1.50 IU in 9 h. (From STEFFENS, 1969a.)

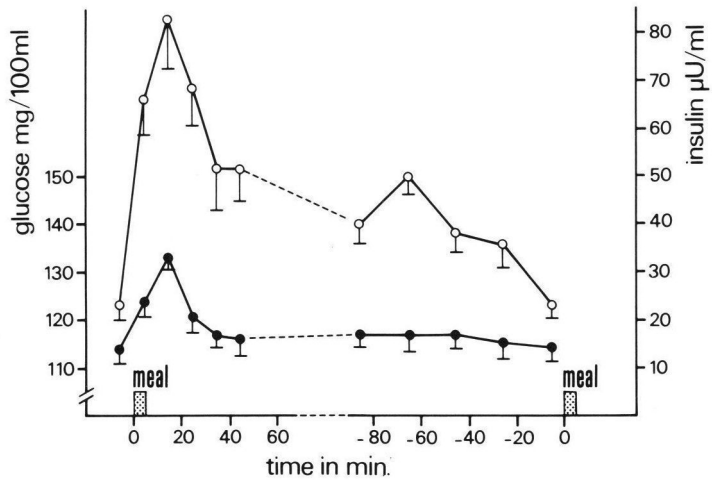

Fig. 6. Average meal and interval cycle of rats: ○—○ insulin; ●—● glucose. (From STRUBBE *et al.*, 1977.)

FENS, 1969a) starts feeding each time that the ensuing hypoglycaemia reaches a critical value (fig. 5). This value, however, is far below the normal physiological range of the blood sugar level. Hence, although it is clear that an emergency signal "hypoglycaemia!!" can trigger food intake, we cannot conclude yet that blood glucose is a satiety factor under normal conditions.

In the undisturbed rat with food at libitum, feeding behaviour is not heralded by a decline of blood sugar (STEFFENS, 1969b), but by the fact that the insulin concentration (fig. 6) drops to a fairly precisely defined value (STRUBBE, 1975; STRUBBE *et al.*, 1977). Secretion of insulin is geared to the blood glucose concentration, and the cells of the body can absorb glucose only if insulin is present as well. In other words, the degree of availability of glucose can be inferred from the insulin concentration, and it is known that insulin reaches the VMH. Could insulin be the agent we are looking for? Support for this view lies in the fact that injection directly into the VMH of a tiny amount of insulin antibody causes temporary hyperphagia (fig. 7), whereas similar injections elswhere in the brain (*e.g.*, in the LH) have no significant effect (STRUBBE & MEIN, 1977). However, we do not know whether this treatment lowers insulin concentration in the VMH to levels beyond its normal physiological range.

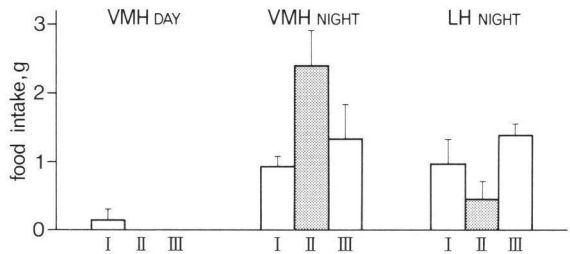

Fig. 7. Effect of injection of antibody to insulin in the VMH or LH on food intake (g). I, II, III: Successive one hour periods; the injection is made at the beginning of II. (From STRUBBE & MEIN, 1977.)

Stronger evidence that glucose availability - as indicated, *e.g.*, by insulin - normally governs food intake would be obtained if it could be shown that high levels of these two substances in the blood are sufficient to keep feeding behaviour in abeyance. However, when such a state is maintained for 90 minutes by means of glucose infusion, food intake of the rat (table I) is not different from that of control animals (STRUBBE *et al.*, 1977).

Similarly, in an extensive study of regulation of food intake in the goat, DE JONG (1981) obtained no proof that circulating volatile fatty acids - the main fuel for metabolism in ruminants - provide satiety signals controlling timing or size of separate meals.

To sum up, the facts presented so far provide no final answer to the problem of the nature of humoral satiety signals. It is true that recently other humoral agents, notably intestinal hormones, have come under

TABLE I

Effects of glucose infusions on meal size, meal duration and duration of the intermeal period (infusion began 2 min after end of first meal).

	Meal I		*Meal II*		*Duration of the Intermeal Period*	
	Size (g)	*Duration (min)*	*Size (g)*	*Duration (min)*	*(min)*	*N*
Without infusion	1.8 ± 0.2	3.5 ± 0.4	1.8 ± 0.2	3.5 ± 0.3	43.7 ± 3.3	18
Saline 83 µl/min	2.0 ± 0.2	3.5 ± 0.3	1.9 ± 0.2	3.4 ± 0.4	50.9 ± 6.9	12
Glucose 8.3 mg/min	1.6 ± 0.2	3.1 ± 0.3	1.8 ± 0.2	3.0 ± 0.4	47.5 ± 4.4	12

scrutiny in this context in several laboratories, including our own (for a short survey see DE JONG, 1981), but again it is not yet clear how and to what extent these may govern food intake.

2.3. *Multifactorial Control of Feeding Behaviour*

In the above we have emphasized signals reporting availability of fuel for the cells, but it is generally envisaged that nervous and humoral messages reporting the presence of food in the digestive tract and the amount of fat in the adipose tissues, also take part in the control of feeding. In addition to these negative feedbacks, positive feedbacks appear to be involved as well (WIEPKEMA, 1971; see section 3.2.2.). Any eventual theory of the control of food intake must certainly be multifactorial (fig. 8). However, concrete data on the influence of any one of the factors mentioned are less plentiful than one could wish. In consequence a number of competing theories have sprung up in the past decades and exist side by side (for a survey, see BOOTH, 1978). Several authors have cast their respective views in the mould of systems theoretical models, but even these often suffer to some extent from vagueness and arbitrariness. In our laboratory several attempts have been made to define precisely where the competing theories disagree, and to devise experiments that may settle these issues (GEERTSEMA, 1973; GEERTSEMA & REDDINGIUS, 1974 SCHILSTRA, 1978, 1983). However, this is not the place to discuss these methodological studies.

2.4. *Marginal Conditions: Interactions Between Feeding and Other Behaviour*

We will now address the question why the influence of messages to the brain reporting the amounts of fuel in the body is so hard to detect in behavioural work. We shall argue that this is so because many other factors enter into the decision whether or not food will be taken at a

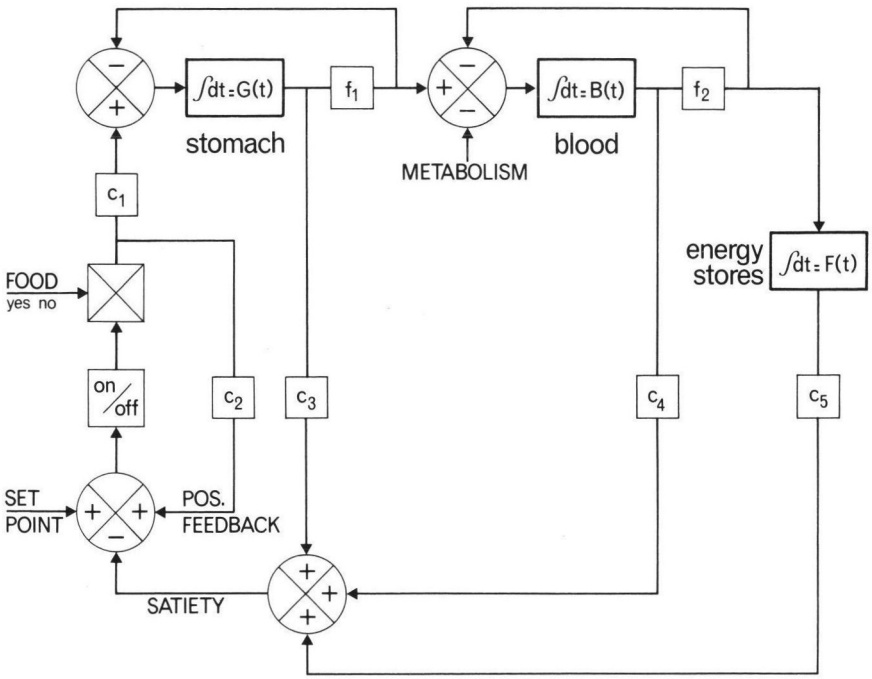

Fig. 8. Systems theoretical representation (designed by A. J. Schilstra) of multifactorial control of food intake. This model, based on ideas of GEERTSEMA & REDDINGIUS (1974), underlies much of our present work. The basic principle is that the amounts of nutrients (energy) present in stomach, blood, and reserves are compared with a set point by the brain, which then decides whether feeding behaviour will be performed. For details, see SCHILSTRA, 1978, 1983.

given moment. For a proper understanding of this point it is important to realize that fluctuations in the tendency to feed occur on a time scale encompassing six to eight orders of magnitude. At one end, there are seasonal variations, such as the increased uptake of hibernators in the months preceding winter, or of migrating species before the long voyage. The biological function of these changes is obvious, but what concerns us here is that the increased uptake cannot be explained from a current lack of energy in the body. At the other end of the scale are fluctuations that take an hour or so, e.g., those causing the pattern of meals and intervals (section 3.1.1.), or even only a few minutes or seconds, *e.g.*, those underlying the details of behaviour during the meal (section 3.2.). Between these extremes there are rhythms such as the four-day periodicity in feeding behaviour linked to the oestrus cycle in the female rat: during oestrus she eats little and is hyperactive,

so that she loses body weight; during dioestrus she eats more so that the losses are made good. Perhaps most marked of all is the daily rhythmicity of feeding. We shall discuss this first.

2.4.1. *Daily rhythmicity*

Feeding in rats is largely restricted to the dark hours. It is not spread evenly over the night (fig. 9). For instance, there is a peak in feeding-activity just before dawn. At that time the digestive tract is well filled.

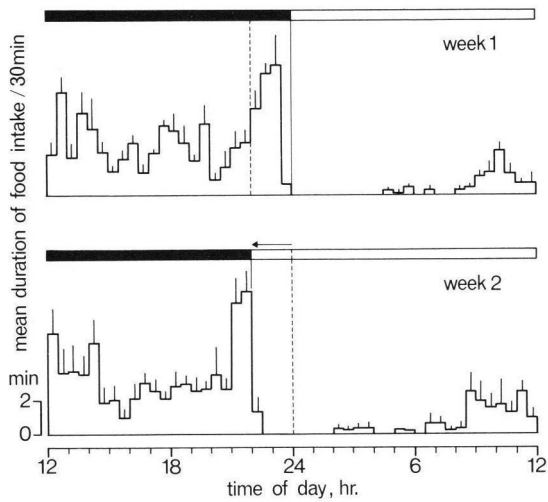

Fig. 9. Mean duration of food intake per 30 min of rats during dark (black horizontal bar) and light (white bar). At the beginning of week 2 light onset was advanced by 2 hours. (From KERSTEN *et al.*, 1980).)

The peak cannot be plausibly ascribed to any lack of fuel in the rat. On the other hand, if the night is shortened by switching on lights 2 h before dawn, the rat promptly adjusts its behaviour by performing the peak two hours earlier as long as the new light regime is maintained. In contrast, the peak is not moved forward when the food is removed from the rat's cage during the final two hours of the night without a change of light regime (fig. 10). Apparently the occurrence of the predawn feeding peak is governed not by the rat's experiences as regards availability of food, but by its expectation as to the duration of the dark period. In this case feeding behaviour is mainly determined by an influence that bears no relation to current energy content (KERSTEN *et al.*, 1980; SPITERI *et al.*, 1982; STRUBBE, 1982).

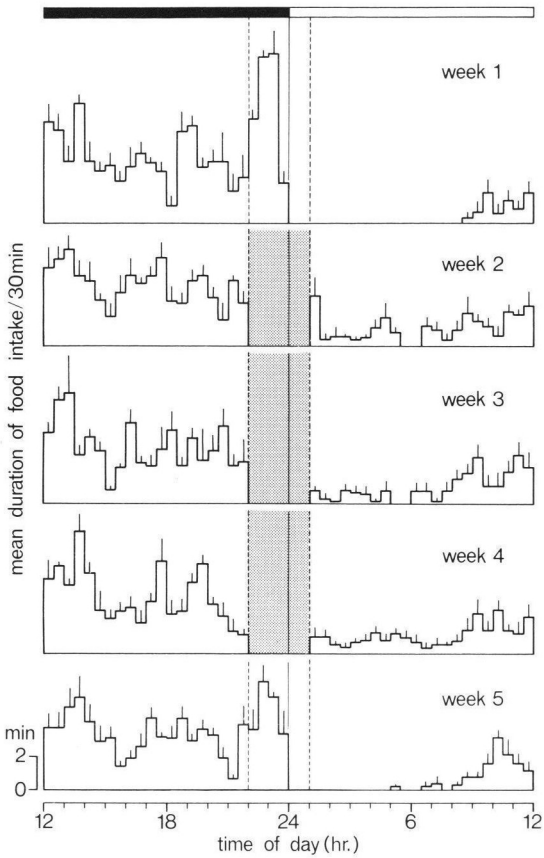

Fig. 10. As fig. 9, but with constant light regime and — during weeks 2 to 4 — three hours food deprivation (stippled). (From KERSTEN *et al.*, 1980.)

2.4.2. *Interaction of motivations*

A further case where feeding behaviour is "bent" by factors not related to energy differs from the foregoing in that 1) the time scale is measured in minutes, and 2) we are dealing not with activation but inhibition of eating. Local injection of the general anaesthetic Nembutal inactivates the VMH of a male rat during some ten minutes; thereafter normal functions return. As expected, the rat manifests hyperphagia during VMH anaesthesia (fig. 11) when it is in a cage with food. However, if an oestrous female is put into the cage as well, feeding behaviour is practically absent. Apparently it is inhibited by the simultaneous activation of sexual behaviour (PROP-V.D. BERG *et al.*, 1977). Ethology has revealed countless other examples of modulation

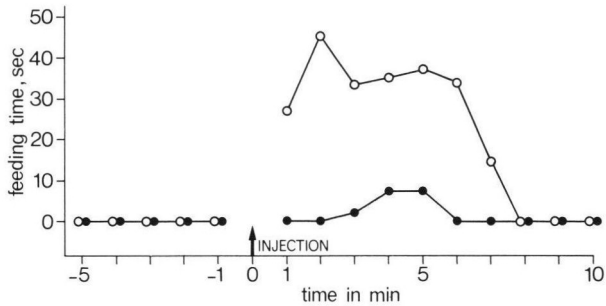

Fig. 11. Nembutal anesthesia of the VMH in a male rat results in hyperphagia (○—○), unless sexual behaviour receives priority due to presence of an oestrous female (●—●). (From PROP-VAN DEN BERG *et al.*, 1977.)

of one behaviour system to suit the requirements of another one. In most cases this takes the form of mutual inhibition (the outcome depending on the relative strengths of the motivations involved), but sometimes positive interactions occur. The range of time scales of such interactions is very wide. It is beyond doubt that they are of the greatest importance for the causal explanation of behaviour (BAERENDS, 1976).

2.4.3. *Towards a more realistic model of feeding behaviour*

It follows from the above that the model that we and others took as the starting point of our search for signals governing feeding is too simple. As fig. 12 illustrates, it assumes that the tendency to perform feeding

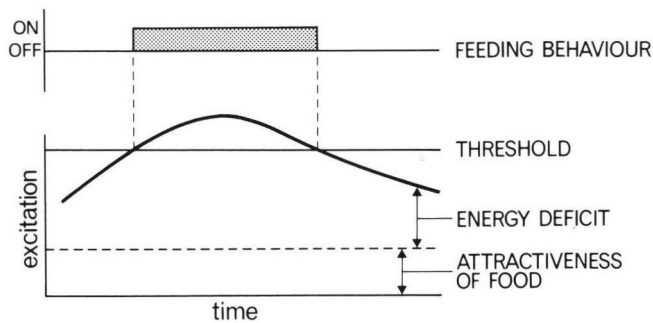

Fig. 12. Simplistic view of the decision process governing food intake. Explanation, see text. Note that the more attractive the food, the lower the degree of hunger required for feeding to start. Excitation may continue to rise for some time after the start of feeding due to the digestive delay between eating and absorption of nutrients into the blood.

behaviour is determined by the sum of a) internal "specific motivational signals" (reporting energy deficits), and b) the external food stimuli (which can be kept constant under experimental conditions). Feeding occurs whenever this sum exceeds a certain threshold, and in consequence motivation will decrease sooner or later until excitation drops below the threshold, whereupon feeding responses cease. The facts mentioned in the previous two paragraphs necessitate revision of this model. We here propose a representation (fig. 13) in which the interferences by other motivations are expressed as fluctuations of the threshold, or — in terms of the model of fig. 8 — fluctuations of the set

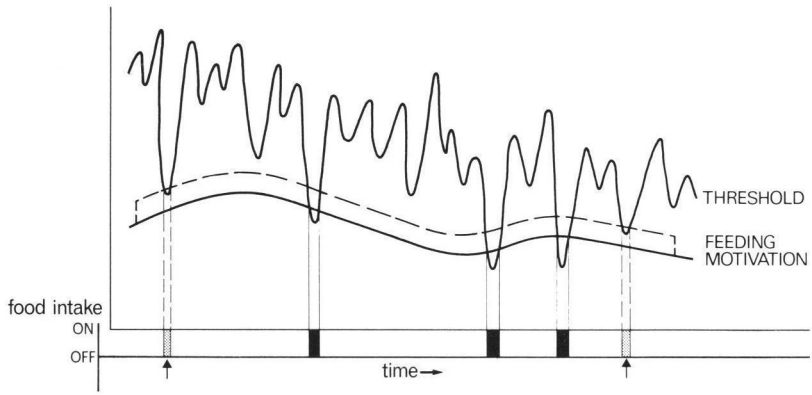

Fig. 13. A more realistic view of the decision process governing food intake (attractiveness of food left out of consideration). See text. During a prolonged experimentally imposed increase (broken line) of the feeding motivation only two meals take place that would not have occurred naturally. The rest of the meals is governed mainly by the fluctuations of the threshold, so that the experimental interference does not noticeably affect their timing.

point. This is an arbitrary choice; a different but equivalent representation can be constructed (SCHILSTRA, 1983) in which the threshold or set point is assumed constant, and the fluctuating factors are regarded as components of the motivation. This amounts, of course, to extending fig. 8 by explicitly incorporating factors now 'hidden in the set point'. Irrespective of which version one prefers, the fluctuations have important implications for the behavioural physiologist. This may be seen as follows.

Some workers, whose main interest is the homeostatic aspect of food intake, want to single out the effect on timing and size of meals of the 'specific' motivational messages that report the energy supplies of the body. For them the fluctuations are mere 'noise'. The amplitude of

the variation in the specific signals and that of the noise are of the same order of magnitude. This is the reason why the behavioural effects of short lasting manipulation of specific motivations are hard to detect. This led DE JONG (1981) to state, at the end of his work on food intake in the goat, that "the effects on food intake of changes in the energy stores of the body or the energy content of the diet become manifest only in the long run. ... This implies that measurements should be made over ... a week rather than a day." This is a crippling requirement, for prolonged manipulation of one potential specific signal is likely to have repercussions for other metabolic and endocrine agents, which may also have signal functions.

For other workers, who focus on the causes of behaviour, fluctuation in effectiveness of specific signals is just as interesting as these signals themselves, for it reflects the limitations other vital functions impose on the performance of feeding. They will aim at unravelling the complex causes of the fluctuations. This reveals regularities as mentioned, *e.g.*, in section 2.4.1., 2.4.2. and 3.2.2. It will also reveal the general importance of 'habit formation' in feeding behaviour, which lies outside the scope of this paper.

3. THE TEMPORAL STRUCTURE OF FEEDING BEHAVIOUR: MEALS AND INTERVALS

3.1. *The Meal as a Functional Unit*

As we shall presently see, detailed analysis of the time structure of food intake is illuminative. In the rat, as in many other mammals, a striking characteristic of this structure is that feeding tends to be concentrated in periods of 10 to 20 minutes, the meals, separated by intervals of an hour or more that are virtually devoid of feeding (fig. 14). This meal-interval pattern is maintained under a wide variety of conditions, as can be seen, *e.g.*, in the female rat during gestation and lactation (fig. 15). Extreme demands are then made on the energy supply. These the female meets, in the order indicated, by 1) increasing meal size up to the point where stomach volume presumably draws the line, 2) increasing meal frequency during night, and finally, when these two measures are no longer sufficient, 3) forsaking daily rhythmicity and eating more meals during day. Nevertheless, the meal-interval structure is maintained throughout (STRUBBE & GORISSEN, 1980).

3.2. *The Causal Background of the Meal Pattern*

From a functional viewpoint the concentration of feeding behaviour in meals makes sense: other behaviour functions can be performed in the

intervals between meals. Mutual interference of feeding and other functions is thereby avoided. But to what causal process is the meal pattern due? Even during the meal feeding behaviour has no strict monopoly: 'feeding bouts' alternate with brief 'gaps' devoted to other activities (fig. 16). What statistical criteria one can use for realiably distinguishing meals (including gaps) and intermeal intervals (possibly containing a few scattered feeding movements) has been discussed, *e.g.*, by METZ (1975). We shall not go into that problem here. What

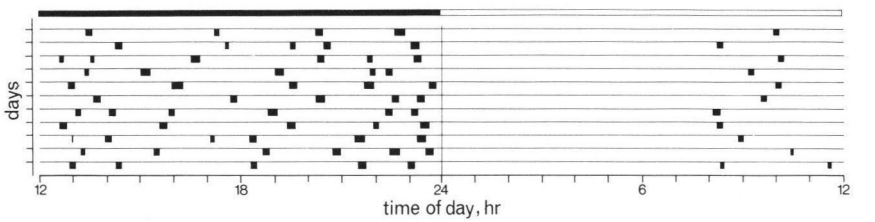

Fig. 14. Daily meal pattern of one representative rat during 11 successive days. (From data of SPITERI *et al.*, 1982.)

matters in the present context is that during the meal the probability is high that the animal will respond to external food stimuli with feeding activities, and that in the interval between meals this probability is very low. As a first approximation it seems reasonable to conclude that the animal can be in either of two distinct internal states (DE RUITER *et al.*, 1974; METZ, 1975), and that the transitions from the 'meal state' to the 'interval state', and *vice versa*, are strikingly sudden (fig. 17). It is not probable that such abrupt changes can be due to an equally sudden outbreak or disappearance of an energy deficit in the body. Two other possible causes come to mind, motivational interaction and exteroceptor feedbacks. The former is rather weakly documented (section 3.2.1.) the latter is better substantiated (section 3.2.2.). Both together may determine the feeding pattern.

3.2.1. *Suppression of inhibition*

In section 2.4.2. we have seen the prevalence of mutual inhibition between different behaviours. Quite conceivably this may lead to a positive feedback cycle whereby if one of two competing behaviours is slightly more activated than the other, the former will somewhat inhibit the latter, and thereby the former will partly remove the negative influence the latter exerts on it. The position of the dominant competitor is thereby further strengthened, and so on (DE RUITER &

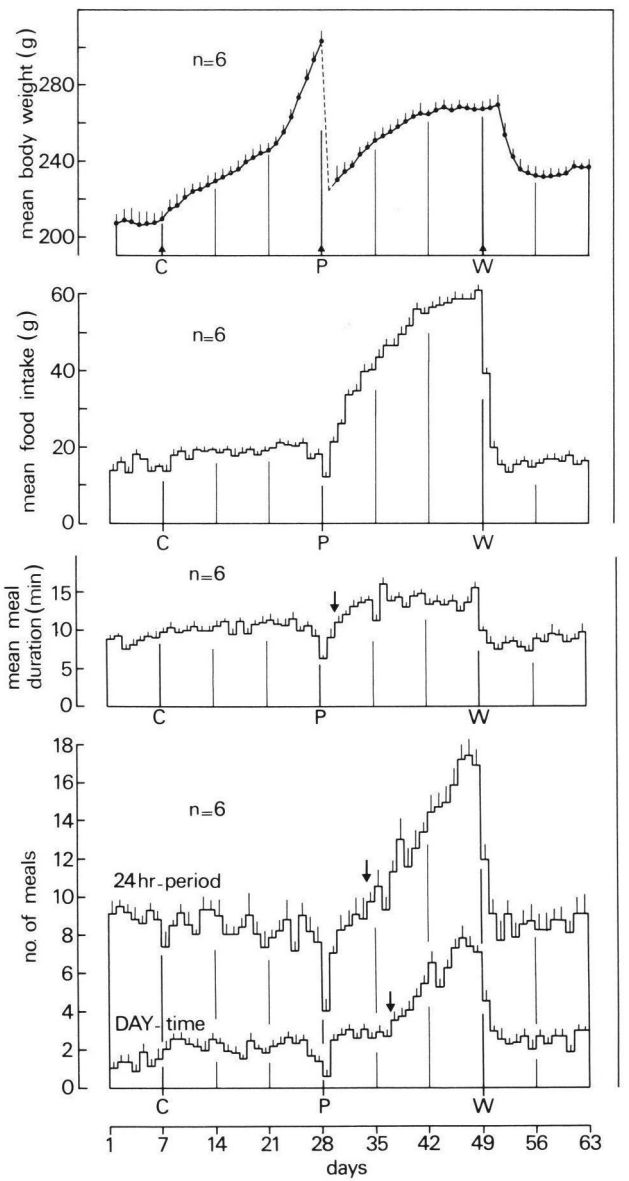

Fig. 15. Daily means (in 6 female rats) of body weight, food intake, meal duration and frequency, during: a control week, 3 postcoital weeks (C = coitus), 3 weeks post partum (P = partus), and 2 weeks after weaning (W). Arrows mark changes in food intake strategy. (From STRUBBE & GORISSEN, 1980).

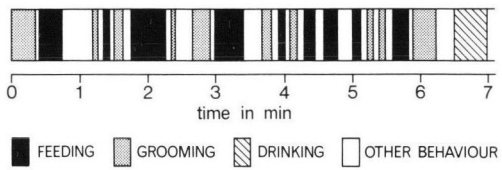

Fig. 16. Fine structure of behaviour during a meal.

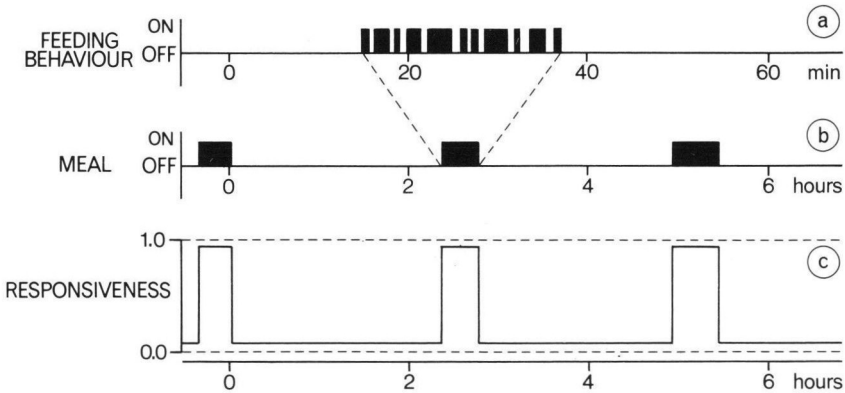

Fig. 17. Changes in responsiveness to external food stimuli during the meal-interval cycle, see text.

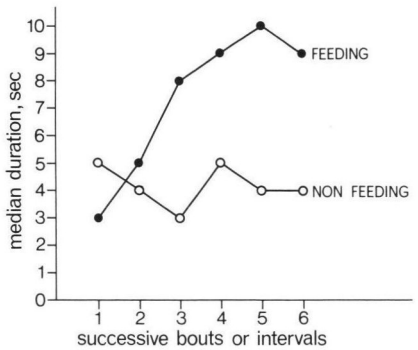

Fig. 18. Duration of first six successive feeding bouts (●) and gaps (○) in the first meal after 24 h fasting (median values of 42 meals). (From WIEPKEMA, 1971.)

WIEPKEMA, 1969). However, we have no hard facts to support this plausible hypothesis.

3.2.2. *Changing appreciation of the palatability of the food*
Feeding behaviour certainly has 'satiating' effects. In addition it may — at least in the early phase of the meal — result in an increase of the tendency to eat. This conclusion rests on detailed analysis of the duration of feeding bouts (WIEPKEMA, 1971). As fig. 18 shows, median bout length increases over the first half dozen bouts of a meal, whereas the duration of gaps does not change. Average bout length depends on the strength of the subject's tendency to go on feeding rather than switch to some other behaviour (see also section 4.2.2.). *i.e.* it is a measure of the feeding motivation. Wiepkema has also shown, by manipulating the taste of the food, that the 'induction of appetite' early in the meal is caused by gustatory stimulation. It occurs only if the food is sufficiently palatable to the eating subject.

A further complication is that this 'appetite' effect of food intake interacts with the 'satiety' effects discussed above. The same gustatory stimulus that in a hungry animal increases the feeding tendency has the opposite effect in a satiated individual. This effect, well documented by other investigators in human feeding behaviour, was also striking in our parabiotic rats (section 2.2.). The rat that was flooded with satiety signals by its gorged twin not only refrained from eating but gave clear signs that it found food repulsive. Our data on mice and on threespined sticklebacks (THOMAS, 1976) indicate that the persistence of the motivational effects of orosensory stimuli is brief. It is measured in seconds, or at most a few minutes. Yet their behavioural effect will be clearcut. For, if the signals reporting energy supply change gradually, as they almost certainly do, the positive and negative orosensory signals will ensure that nevertheless the transitions from interval to meal, and vice versa, are nearly steplike.

Finally, the influence of learning processes, though not directly relevant to the meal pattern problem, cannot be omitted from a discussion of palatability. We have so far considered the case that only a single type of food is present, but many animals meet a range of different food objects in their natural habitats. Moreover, the menu may change with time. In such cases, as shown by BEUKEMA (1968) for the stickleback, the responsiveness of the feeding individual to any particular food is affected by learning. Not only must the fish learn to detect a new prey. Even more interesting is that experience of the taste of a new prey causes a reset of the palatability ratings the fish gives to other prey present in the habitat. Thus, even when it never sees more than one food object at a time, an animal may base its decision

whether to eat or reject that object not only on its current degree of hunger or satiety, but also on its expectation of what other food it will find if it goes on searching. In other words, palatability or attractiveness of a food object (fig. 12) is not an absolute but a relative quality and subject to modification by learning.

4. IN SEARCH OF THE BRAIN MECHANISMS UNDERLYING TEMPORAL PATTERNING OF BEHAVIOUR

4.1. *Starting point: a Synoptic Model of Overt Behaviour*

As stated in section 1 we are not aiming at elucidation of the sensory and motor functions of the central nervous system (CNS) required for the performance of any elementary activity — subjects on which physiology has booked great advances in recent decades. Rather, we seek to explain the order in which the various behaviours are performed one after another. In other words, our work is directed at the physiological mechanisms that enable the animal to decide what it must do next, and to take that decision on the basis of all data available to the CNS, including currently incoming messages as well as previously stored information.

Any insight in this matter will have to rest on a synoptic description of the temporal structure of behaviour that brings out relevant aspects of the decision process. It is our working hypothesis that a description of behaviour as exemplified by the description of feeding in section 3 is eminently suitable for this purpose. We have adopted this hypothesis on the basis of observations, by ourselves and others, of a broad spectrum of behaviours in the rat. While convinced that further ethological foundation (especially through observations outside the laboratory) is desirable, we feel justified to assume that such behaviours as, for instance, drinking, sleeping, grooming, mating, or agonistic behaviour, just as much as feeding, may be said to be concentrated in "episodes" (to coin a term that will serve for all behaviours to indicate what we have so far called meals in feeding). These episodes are separated by intervals virtually devoid of the behaviour that is preponderant in the episode. Within an episode 'bouts' of the preponderant behaviour may alternate with 'gaps' taken up by some other activity. Behaviour as a whole may be viewed, in first approximation, as a succession of episodes of different types. The number of different types of episodes is limited.

In our brain research we assume that occurrence of an episode of a given type corresponds with a particular functional state of the CNS. This state is characterized by high responsiveness to a particular set of

aspects of the external stimulus situation (*e.g.*, "food", or "female"), so that a particular class of responses predominate in overt behaviour. However, other elementary activities are interspersed; *i.e.*, responsiveness to other aspects of the external situation, though slight, is not zero. In sum, on this view we may attempt to characterize the functional state of the CNS by specifying responsiveness to the appropriate external stimuli for all of the elements that together constitute the behaviour repertoire.

This approach differs from that which starts by dividing the repertoire into behaviour systems (section 1) and then attempts to explain the time pattern of activities in terms of specific motivations and their interactions. No doubt models of the latter kind have proved of great value to the development of ethology. The reason for our change of strategy lies in difficulties inherent in the definition of 'behaviour system': "Such a system comprises the set of elements that share a common set of internal factors" (DE RUITER & WIEPKEMA, 1969: 460), or — more precisely — a common set of specific internal motivational factors (*l.c.*, p. 466). The difficulties, which stem from details revealed by the increasingly refined observations of ethologists, were summarized by us some fifteen years ago (DE RUITER, 1967) in a diagram (fig. 19). They soon made us realize that "if we aim at prediction of the behaviour pertaining to some system, it will not do to base our attempt on analysis of the specific motivation of that system alone. We must include ..... the state of other systems ..... and their effects on the system on which we focus our interest" (DE RUITER & WIEPKEMA, 1969: 468). Our above discussion of constant or fluctuating thresholds (section 2.4.3.) states the same view in different words.

It is not surprising, therefore, that we encountered obstacles when we tried to interpret the results of some of our physiological work in terms of behaviour-systems models (section 4.2.1.). Moreover, we felt that a model of behaviour in terms of specific motivations may tempt one to think of the brain in terms of relatively discrete, specific centres, or networks, each subserving a given motivation. Yet it seems safer, when dealing with the brain, to avoid such preconceived ideas as much as possible. For the present, therefore, we prefer to aim at a description of the state of the CNS in terms of a "spectrum" of responsiveness. This has the added advantage that it avoids the methodological pitfalls of distinguishing between altered motivation and effects on learning, for it provides a terminologically almost neutral statement of the effects of manipulation of the brain in terms of changes in the subject's responsiveness to each element out of a large set of stimuli. On the other hand we do realize that serious methodological and practical obstacles will yet have to be overcome along this road.

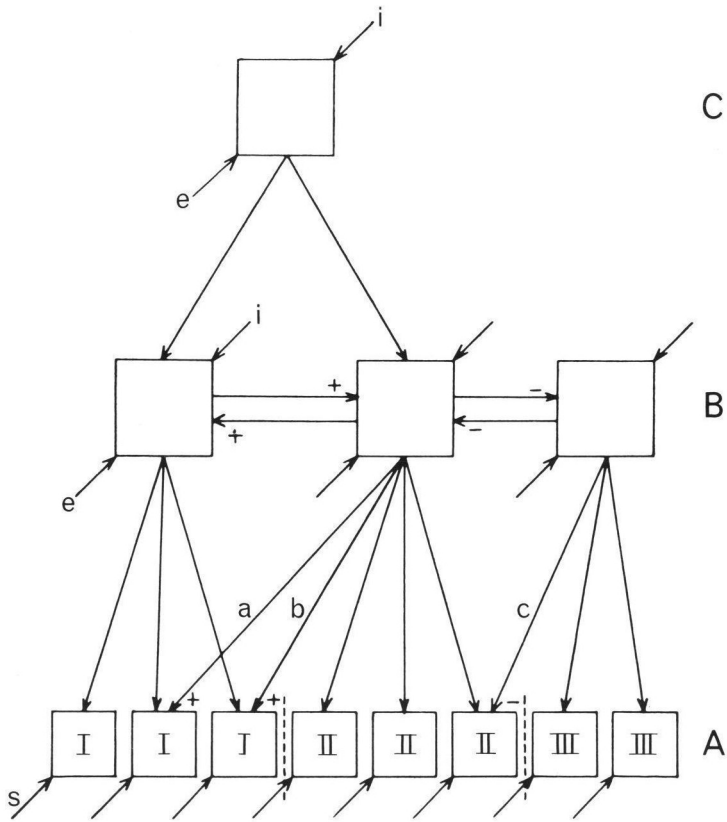

Fig. 19. Some complications envisaged in ethological analyses of behaviour systems. Level A: elementary activities (I, II, III: three different behaviour systems); level B: "specific" motivational mechanisms; level C: higher order motivational mechanism. If only some of the elements of a system are activated (+) or inhibited (-) by the motivation of other systems, this can be symbolized as by a, b, and c. Parallel or inverse fluctuations of entire systems can be ascribed to interactions at level B, or to influences from level C. Each motivational mechanism is influenced by internal (i) and external (e) signals. Each elementary activity has its specific releasing stimuli (s). (From DE RUITER, 1967.)

4.2. *A Few Examples*

4.2.1. *Specific networks for behaviour systems in the VMH?*

A study by OLIVIER (1977a, b) exemplifies the difficulties into which an approach in terms of behaviour systems and specific networks may lead. When confronted with another male, a male rat may show a variety of 'agonistic' responses, ranging from overt attack over different patterns of threat to flight or submission. Following earlier

authors, Olivier has divided these behaviours into two categories: offensive and defensive. He further assumed, though not quite explicitly, that offensive and defensive motivational mechanisms may be distinguished in the CNS. Similarly, Koolhaas and collaborators (KOOLHAAS *et al.*, 1980) regard offensive behaviour as a behaviour system, and summarize their views of its structure in a systems theoretical diagram, which they present as a starting point for physiological analysis. Such models are fraught with problems (*cf.* fig. 19). Olivier himself points out that the movement called frontal threat is "a hybrid under the control of both offensive and defensive

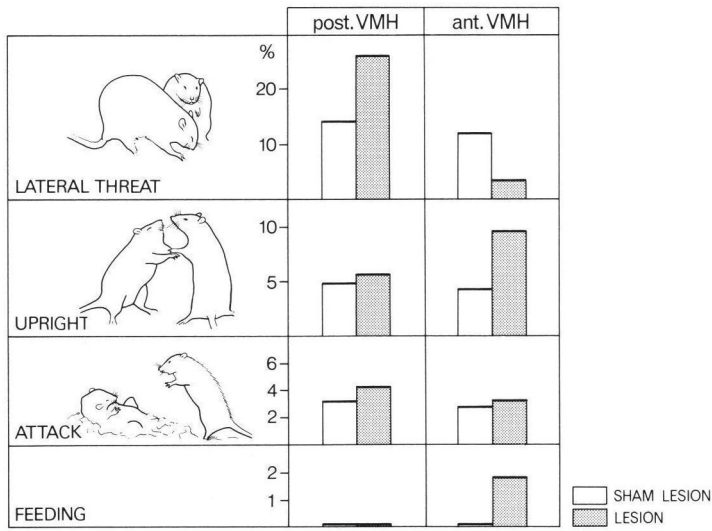

Fig. 20. Changes in the percentage of time spent by a male rat on various activities after lesions in the anterior or posterior VMH. (From OLIVIER, 1977a, b.)

mechanisms". He also emphasizes "the overriding influence of the external stimulus situation. Not only the frequency but also the sequential patterning of behaviour of the experimental male varied greatly with its respective role as territory owner or intruder".

In his brain experiments Olivier made lesions either in the rostral or the caudal area of the VMH. The former biased behaviour towards offense, the latter towards defense (fig. 20). In addition, depending on its site, a lesion might cause hyperphagia, or a reduction of exploratory behaviour, or changes in sexual activity. These effects were mutually independent. Discussing his findings in terms of behaviour

systems and specific networks, OLIVIER (1977a) concludes that "the rostral area of the VMH contains at least three independent neural systems for the regulation of a) feeding behaviour, b) defensive behaviour, c) sexual behaviour" and "the caudal area at least two independent neural systems, respectively for a) feeding behaviour and b) offensive behaviour". His definition of "specific and unrelated neural mechanisms" is "mechanisms specifically underlying one and only one behaviour system". OLIVIER (1977a) himself is careful to call attention to the cumulative uncertainties inherent in the consecutive steps of the proof that such mechanisms exist. What eventually gives him some confidence in this approach is the fact that specific sensors for the detection of motivational signals (*e.g.*, gluco-, osmo-, androgen receptors) have been demonstrated in the VMH and elsewhere in the brain. However that may be, his final conclusion is "that further work is needed for the interpretation of (his) findings in terms of neuronal processes subserving behaviour in the intact animal."

4.2.2. *The VMH a decision generator?*

VEENING (1975) has tried another approach to explain the effects of electrical stimulation of the VMH on male rat behaviour. He, too, used a synoptic description of normal, undisturbed behaviour, but this was not based on behaviour systems and specific motivations. As his starting point he took a record, as complete as possible, of all activities of his male rats in situations where feeding behaviour alone, or alternating with agonistic or sexual behaviour, could be performed. On these data he carried out a first order sequence analysis. The results of this gave grounds for distinguishing, in normal behaviour, three preferred sequences: a feeding, an agonistic, and a sexual sequence. Each sequence consists of a number of different elementary activities in a well defined order (fig. 21). When the rat embarks on a sequence, this may be broken off before completion (in which case the animal may start a different sequence, or revert to an earlier link of the same one). As the number of links of a sequence that have been carried out increases, the probability that the rat will go on to the next link also goes up. One activity, called scanning by Veening, occupies a special position. It is seen especially after completion or interruption of a sequence: it appears to be an overt sign that the rat is in the process of deciding the nature of the next sequence it will start. If these decisions result in a choice for the same kind of sequence several times in succession, the result is a "bout" of sequences of that kind of behaviour. Clearly, the orderly structure of behaviour emphasized by Veening has a time scale shorter by at least one order of magnitude than the

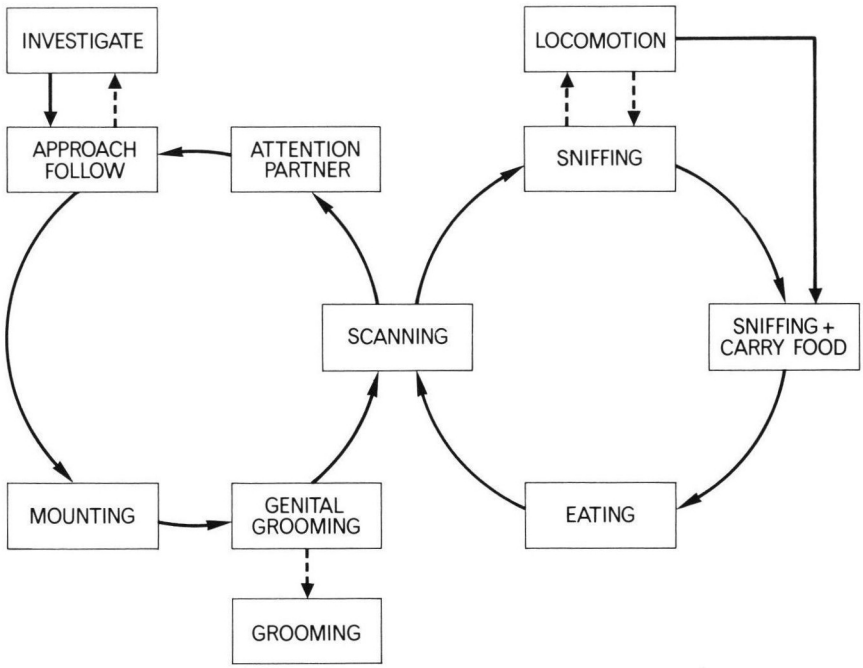

Fig. 21. Feeding cycle and sexual cycle in the behaviour of a male rat. Note the intermediate position of scanning; see also text. (After VEENING, 1975.)

episodes mentioned in section 4.1.: Veening is dealing with the fine structure of the bouts and gaps of which the episodes consist.

A similar analysis of behaviour during unilateral VMH stimulation revealed profound changes in the sequential structure. Sequences are broken off in the initial stages much more often, duration of the terminal link of the chain is greatly reduced, and the mean duration of scanning is much longer than in control periods. After weighing several alternatives Veening concludes that the VMH plays a role in the decision what kind of sequence must be carried out at a given moment, *i.e.*, that it is involved either in the transmission or the evaluation of messages relevant for that decision. In Veening's view the disturbance seen during electrical stimulation may "be due to reduction of positive, or an enhancement of negative motivational signals for all of the various behaviours. In any case, the result is that the ability to make decisions for any sequence of behaviour is attenuated". As he points out himself, his "results are equally compatible with the hypothesis ..... of discrete, but interwoven neuronal

networks as with (that of) .... a unitary neuronal system subserving, *e.g.*, interaction between behaviour systems.'' The latter possiblity is further elaborated in DE RUITER *et al.*, (1974).

4.2.3. *The amygdala and agonistic behaviour*

Our final example concerns one aspect of a study of the effects of lesions in the corticomedial amygdala of a male rat on its agonistic behaviour towards a male conspecific (BOLHUIS *et al.*, 1984). If the experimental animal has no previous experience of its opponent, its behaviour during the confrontation alternates between approach and avoidance. If it has previously been badly defeated by a dominant opponent, it will show practically only avoidance when it comes across this opponent again on subsequent days. However, after elimination of its corticomedial amygdala, the effect of a previous defeat is no longer noticeable on later days. It must be emphasized that in this ex-

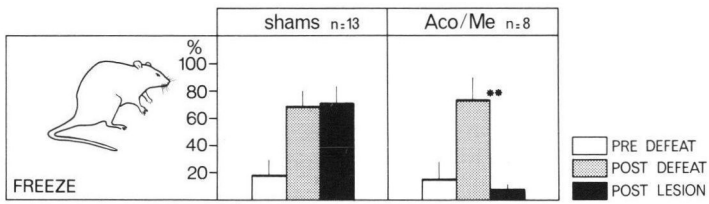

Fig. 22. Effect of sham and corticomedial amygdala (Aco/Me) lesions, made after severe defeat, on the behaviour change due to this defeat in a subsequent aggressive interaction. (After BOLHUIS *et al.*, 1984.)

ample the time scale of the behaviour changes is much longer than in the previous ones. Several different explanations may be envisaged. Not only have the obvious alternatives been suggested, either that the lesion has disrupted the mechanism of memory, or that it has strengthened the aggressive (*c.q.* weakened the escape) motivation (fig. 22). At least five different, partially overlapping theories of the functions of the amygdala can be found in the literature. A critical review lies outside the scope of this paper. We mention merely that BOLHUIS *et al.* are inclined to interpret their findings in terms of disturbed memory functions, because the lesion also brings about comparable changes in other behaviours. This illustrates that broad screening of behaviour may provide a solution for dilemmas like the present one.

5. A TENTATIVE CONCLUSION

How is the VMH, or any other anatomically or neurochemically defined subdivision of the brain, geared to the functioning of the CNS as a whole? How and where in the CNS do neuronal activity patterns change when, for instance, foraging behaviour makes way for parental care? No real answers to these questions are forthcoming yet, in spite of decades of excellent research in many institutes. This is not to deny that the efforts have yielded much insight in the wiring of the CNS, in neuronal transmission, in electrophysiological activity patterns in certain networks in relation to the functional state of the CNS as a whole, in information processing in sensory systems, in the cybernetics of motor functions, in the role of glia, in the physical and chemical backgrounds of learning processes, and so on. The real difficulty, however, is of an altogether different nature. It is not a problem of the "hardware" of the CNS. Even if we knew every detail of the properties of its elements and the way in which they are wired up, this would not explain precisely how the CNS operates during any given behaviour, nor how it can change its own input-output relations in such a way that the individual responds now to this and the next minute to another aspect of its environment, always with functionally appropriate behaviour. If one looks for an analogy with a physical system, one might perhaps regard the brain as a 'self-reprogramming' supercomputer. But such analogies are only moderately helpful. To solve questions like those just mentioned, a new generation of brain research will be needed, to which many disciplines will have to contribute. An obstacle on this path is that the relations between the various conceptual systems of these disciplines are not always transparent. This hampers the interchange of ideas and results. Methodological analysis will be needed to remove this obstacle, but empirical studies will not mark time till the road is clear. What then is the best way to proceed in the meanwhile? Indispensible in any case is a system for the description of behaviour tailored to the special needs of this kind of brain research. Ethology has much to contribute here for at least two reasons. First, because in principle it always considers the entire behaviour repertoire of the individual. Second, because even when dealing with a purely causal problem the ethologist will not lose sight completely of the functional and evolutionary aspects, which puts him in a good position when it comes to generalizing the results of laboratory work to natural conditions. The contributions of ethology will be most useful if couched in terms that do not refer, explicitly or implicitly, to models of the causal structure of behaviour that are of questionable neurobiological applicability. We have given some ex-

amples in this paper of our attempt to achieve this. No doubt this will have to be supplemented with new techniques for data processing (*e.g.*, higher sequence analysis). New developments in biomathematics and linguistics may also contribute to the construction of a really effective system for describing behaviour.

It is clear that behavioural physiology will have to come to grips with problems on different time scales. At one extreme lies the programming of single sequences of elementary activities, at the other extreme the semipermanent changes due to learning. In between we find, *e.g.*, what has here been called the episode structure of behaviour. This we feel is one of the things for research on brain and behaviour to tackle. We have argued above that it is an important functional, adaptive aspect of behaviour. Moreover, we believe that it will prove relatively amenable to (neuro)physiological analysis, because in the CNS sites can be located where the motivational signals are received that determine the succession of episodes (osmoreceptors, androgen receptors, glucoreceptors, *etc.*). What internal and external messages contribute to motivation is a fruitful theme for joint investigation by physiologists and ethologists. Further questions will follow automatically, *e.g.*, on the processing and integration of these signals, and also on their evaluation in the light of information stored in the memory. These events culminate in a decision by the CNS what the next behaviour will be. If we want to elucidate them, we must avoid premature choice of detailed models as a guideline for planning the work. It is better to keep an 'open mind' especially on the question whether the CNS may be regarded as a composite of specific networks, or rather as an indivisible, self-reprogramming whole.

However that may be, we can be sure that the study of brain and behaviour will continue to pose immensely complex problems. Yet for two reasons it cannot be properly called a Gordian knot. Firstly, in this case there is no useful short cut like Alexander's (PLUTARCHUS, *ca.* 96). Secondly, in Gordion "the fastenings had their ends concealed", but in our case ethologist and physiologist each hold one end already. Though the rope be "intertwined many times in crooked coils", we may expect that, given patience and ingenuity, they will manage to disentangle it.

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